

REMARKS/ARGUMENTS

I. STATUS OF THE CLAIMS

With entry of this amendment, claims 1-3, 6-8, 11-13, 16-18, 21-23, 26, 27, 31-36, 39-42, 45-47, 50-52, and 55-81 are pending. Claims 1, 11, 33, 39, 45, and 50 are currently amended and Claims 55-81 are newly added. Support for the amendment to claims 33, 39, 45 and 50, adding the term "recombinant" to clarify the distinction from naturally occurring polymerases, can be found throughout the specification, in particular, at page 7, lines 16-18. The amendment to claims 1, 11, 21, 31, 32, 33, 39, 45, and 50 to recite the Markush group consisting of "*Thermus thermophilus*, *Thermus specie Z05*, *Thermus Specie sps17*, *Thermus caldophilus*, *Thermus filiformis*, *Thermus oshimai*, *Thermus silvanus*, *Thermus chliarophilus*, *Thermus scotoductus*, *Thermus ruber*, *Thermus brockianus*, *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosipho africanus*, *Bacillus caldotenax*, and *Bacillus stearothermophilus*" can be found throughout the specification. In particular, at page 15, Table 1, and at page 17, lines 16-24, of the specification. Support for new claims 55-81 can be found throughout the specification, in particular, at page 15, Table 1, of the specification. No new matter is added.

II. REJECTION UNDER 35 U.S.C. §101

Claims 1-3, 6-8, 11-13, 16-18, 33-36, 39-42, 45-47, and 50-52 stand rejected as being allegedly directed to non-statutory subject matter. The Examiner alleges that the claims do not distinguish over polypeptides and nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and naturally occurring ones.

Applicants traverse the rejection. Specifically, each of the independent claims 1, 11, 33, 39, 45 and 50 recite a recombinant thermostable DNA polymerase. The feature that the thermostable DNA polymerase is recombinant, distinguishes the polypeptide from its naturally occurring state. The specification states that:

The term "native" refers to a gene or gene product which is isolated from a naturally occurring source. This term also refers to a recombinant form of the native protein produced by molecular biological

techniques which has an amino acid sequence identical to that of the native form. (Emphasis added).

See, page 7, lines 16-18, of the specification.

Thus, a recombinant thermostable DNA polymerase is distinguished from the naturally occurring sequence in that it is produced by molecular biological techniques.

In light of the above, and the claims as presently recited, Applicants request that the Examiner withdraw the rejection.

III. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH - WRITTEN DESCRIPTION.

Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, and 50-52 stand rejected as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that the claims have been amended to recite the limitation: "wherein said polymerase is selected from a *Thermus* species other than *Thermus aquaticus*." The Examiner alleges that the specification does not provide support for "any species other than *Thermus aquaticus*." The Examiner indicates that the rejection can be overcome by amending the claims to recite the specific *Thermus* species: *flavus*, *thermophilus*, *specie Z05*, *Specie sps17*, *caldophilus*, and *filiformis* as listed in Table 1.

Applicants have amended the claims consistent with the Examiner's suggestion in view of the species listed in Table 1 and the exemplary species described in the accompanying text on page 17, lines 16-24, of the specification. In light of the claims as presently amended, Applicants request withdrawal of the rejection.

IV. REJECTION UNDER 35 U.S.C. §102(e)

A. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26, 27, 31, 33-36, 39-42, 45-47 are not anticipated by Brandis I (U.S. Pat. No. 6,265,193) under 35 U.S.C. §102(e).

The Examiner cites Brandis I as allegedly teaching, *inter alia*, mutant DNA polymerases having at least one mutation at position 681 with respect to *Taq* DNA polymerase, wherein the mutant DNA polymerase has at least 2-fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring

DNA polymerase. *See*, page 4 of the Office Action, citing claims 1-13; col 6, lines 4-39; col 8; and tables 1 and 2, at cols. 17-22 of Brandis I. Furthermore, the Examiner alleges that Brandis I does not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species including *Thermus flavus* (*see*, page 4 of the Office Action citing col. 8 lines 53-54 of Brandis I).

Applicants traverse the rejections to the extent that they apply to the claims as presently amended. Specifically, independent claims 1, 11, 21, 31, 32, 33, 39, 45, and 50, as presently amended, are directed to recombinant thermostable polymerases selected from the group consisting of: *Thermus thermophilus*, *Thermus specie Z05*, *Thermus Specie sps17*, *Thermus caldophilus*, *Thermus filiformis*, *Thermus oshimai*, *Thermus silvanus*, *Thermus chliarophilus*, *Thermus scotoductus*, *Thermus ruber*, *Thermus brockianus*, *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosipho africanus*, *Bacillus caldotenax*, and *Bacillus stearothermophilus*. Brandis I does not disclose a polymerase from any of the species recited in the independent claims as presently amended. Because Brandis I does not disclose a polymerase selected from a species as presently claimed, Brandis I does not anticipate any of the independent claims.

The arguments as presented above with regard to the independent claims is also applicable to the dependent claims, which include all of the limitations of the independent claim from which it depends.

In light of the above, and the claims as presently amended, Applicants respectfully request that the Examiner withdraw the rejection.

B. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26, 27, 31, 33-36, 39-42, 45-47 are not anticipated by Brandis II (Brandis *et al.* U.S. Pat. Pub. No. 2002/0164591) or Brandis III (Brandis *et al.* U.S. Pat. Pub. No. 2006/0088879) under 35 U.S.C. §102(e).

The Examiner cites Brandis II and III as allegedly teaching, *inter alia*, mutant DNA polymerases having at least one mutation at position 681 with respect to *Taq* DNA polymerase, wherein the mutant DNA polymerase has at least 2-fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally

occurring DNA polymerase. *See*, page 5 of the Office Action, citing claims 1-8, 15, and Tables 1 and 2 of Brandis II and III. Furthermore, the Examiner alleges that Brandis II and III does not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species including *Thermus flavus* (*see*, page 5 of the Office Action citing paragraph [0037] of Brandis II and III.

Applicants traverse the rejection for the same reasons as discussed above with regard to Brandis I. In view of the claims as presently recited, and the arguments presented, Applicants request that the Examiner withdraw the rejection.

V. REJECTION UNDER 35 U.S.C. §103(a)

Claims 32, and 50-52 stand rejected as being allegedly unpatentable over Brandis I, II, or III each in view of Gelfand *et al.* (U.S. Pat. No. 5,939,292). The Examiner cites Brandis I, II, and III, *inter alia*, for the reasons stated above with regard to the rejections under 35 U.S.C. §102(e). The Examiner cites Brandis I, II, and III as teaching the specific E681K mutant, kits comprising the mutant polymerase, and fluorescently labeled nucleotide dyes. Specifically, with regard to claims 32, 50-52, the Examiner cites Brandis I, II, and III as teaching mutant polymerases comprising other mutations in addition to the discrimination mutations such as those at position 681 of *Taq* polymerase, including mutations at position 615 of *Taq* polymerase. *See*, page 7 of the Office Action. The Examiner acknowledges that Brandis I, II, or III do not specifically teach a polymerase comprising both a mutation at position 681 and a mutation at position 615. The Examiner, however, cites Gelfand *et al.* (U.S. Pat. No. 5,939,292) as curing this defect in Brandis I, II, and III.

The Applicants traverse the rejection on the grounds that the Examiner has not established a proper *prima facie* case of obviousness. Specifically, The Applicants contend that the combined references do not teach or suggest all of the limitations of independent claims 32 or 50 as presently amended. In particular, independent claims 32 and 50 as presently amended are directed to recombinant thermostable DNA polymerases selected from the group consisting of: *Thermus thermophilus*, *Thermus specie Z05*, *Thermus Specie sps17*, *Thermus caldophilus*, *Thermus filiformis*, *Thermus oshimai*, *Thermus silvanus*, *Thermus chliarophilus*, *Thermus*

scotoductus, *Thermus ruber*, *Thermus brockianus*, *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosiphon africanus*, *Bacillus caldotenax*, and *Bacillus stearothermophilus*. As discussed above with regard to the rejection under 35 U.S.C. §102(e), neither Brandis I, II, nor III teach or suggest a recombinant polymerase from any of the species as presently claimed. Because the cited references, neither alone nor in combination, teach or suggest all of the limitations of independent claims 32 or 50, the cited references do not render independent claims 32 or 50 as obvious. Therefore, independent claims 32 and 50 are patentable over the cited references.

Claims 51 and 52 depend either directly or indirectly from independent claim 50, and therefore include all of the limitations of independent claims 50. The arguments as presented above with regard to claim 50 are also applicable to dependent claims 51 and 52.

In light of the above, the Applicants request that the Examiner withdraw the rejection.

VI. OBVIOUSNESS TYPE DOUBLE-PATENTING REJECTION

The Examiner has provisionally rejected claim 31 as being unpatentable over claims 13-16, 20-24, 27-32, 36-44, and 48-52 of co-pending U.S. Pat. App. No 09/823,649 (filed March 30, 2001, and assigned to Roche Molecular Systems), in view of Giardano *et al.*(U.S. Pat. No 6,107,029), under the judicially created doctrine of obviousness-type double-patenting.

Applicants request that the provisional obviousness-type double-patenting rejection be held in abeyance until patentable subject matter has been identified in the present application.

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Reply to Office Action of

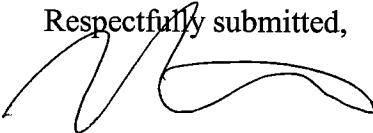
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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